

Appln. No. 09/050,249
Amd. dated March 29, 2005
Reply to Office Action of November 1, 2004

REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 93 and 95-120 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The specification has been objected to for informalities. Appropriate correction, as supported by the context of the paragraph, is made, thereby obviating this objection.

Claims 93-96, 98-117, and 119 remain rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention. The examiner holds that the limitation "a variant thereof which has the same antigenic fragment(s) as in (i) to be used in obtaining said monoclonal antibody" constitutes new matter. This rejection is now obviated by replacing the term "variant" with "homologue" in claim 93 and deleting the above limitation.

Claims 94, 98-117, and 119 remain rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This

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rejection is obviated by the cancellation of claim 94 and the amendment to the dependent claims to change the dependency by deleting any dependence from canceled claim 94.

Claims 93-96 and 98-118 remain rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description. Applicants believe that claim 93, as amended in response to the rejections, obviates this rejection.

Claims 93-120 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Nakamura et al., *Infect. Immun.* 61:64-70 (1993). This rejection is respectfully traversed.

The examiner holds that Nakamura's factor in the serum sample (75 kDa) was the same as IGIF found in the liver extract (19 kDa), and that the higher molecular weight form was considered to be bound to another protein or to exist in an oligomeric form. However, this is mere hindsight. As argued previously, Nakamura's first publication never states what the examiner is asserting. Applicants note that the examiner's position was formed only after taking the information disclosed in Nakamura's later publication (*Infect. Immun.* 63:3966-3972, 1995) into account. Nakamura's later publication however was not published until after the present application was filed.

In order to assert that the presently claimed invention is obvious over Nakamura's first publication (*Infect. Immun.*

61:64-70, 1993), the claimed subject matter had to be made obvious from the disclosure of Nakamura's first publication alone at the time the invention was made. It is worth again noting that Nakamura's later publication was not published at the time the present invention was made. Accordingly, applicants believe that relying on the disclosure of Nakamura's later publication when considering the obviousness of the claimed invention is unreasonable.

Nakamura's first publication states at page 68, right column, lines 12-28:

In the present study, we purified an unidentified soluble protein factor which was able to induce a markedly high level of IFN- γ in spleen nonadherent cells. ...The factor was apparently homogeneous and composed of one unit (Fig. 2).

The purified substance was much smaller by SDS-PAGE (50 to 55 kDa) (Fig. 2B) than by the molecular sieve technique (70 to 75 kDa) ... interaction between other molecules might have been occurred. Alternatively, a small fragment might have been lost during the purification procedures.

The molecular shape may have influenced the result. Since the factor lost its activity in SDS-PAGE, we also failed to definitely establish that the band revealed by SDS-PAGE was the factor. (emphasis added)

It is quite clear that Nakamura's first publication never teaches that Nakamura's factor was in a form bound to another protein or in an oligomeric form.

From the disclosure in Nakamura's first publication as discussed above, it can be said that a factor which was able to induce a high level of IFN- γ might be a single substance, and that said factor having a molecular weight of 50 to 55 kDa on SDS-PAGE might be a decomposed substance of the factor that revealed the molecular weight of 70 to 75 kDa on the molecular sieve technique, and that it might lose its activity due to decomposition.

It can also be said that it might be the "small fragment" lost during the purification procedures that is able to induce IFN- γ . Furthermore, it can be presumed that it might be an unknown component which lost its activity on SDS-PAGE that is able to induce IFN- γ , or that the factor having the molecular weight of 70 to 75 kDa might reveal its activity of inducing IFN- γ due to the interaction between other molecules. In this regard, Nakamura's first publication provides many presumptions and considerations. The position held by the examiner that Nakamura's factor was in a form bound to another protein or in an oligomeric form is one of the presumptions provided by Nakamura's first publication. Applicants believe that the examiner's

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position can be formed only after taking the disclosure of Nakamura's later publication into account and therefore is believed to be a case of hindsight reconstruction.

Applicants also respectfully point out that Nakamura has not succeeded in obtaining a monoclonal antibody specific to IGIF despite the examiner's assertion that it would have been obvious to obtain a monoclonal antibody specific to IGIF over the disclosure of Nakamura's first publication. Nakamura was not successful in obtaining such monoclonal antibody even after the present application was filed, as evidenced by Nakamura's later publication (*Infect. Immun.* 63:3966-3972, 1995) at page 3972, first and second paragraphs, which states:

The cellular origin of IGIF remains unknown...
To resolve this issue, a specific antibody,
monoclonal, if possible, will be helpful.

This will enable a sufficient supply of
recombinant IGIF or the antibody against it
for examination of its biological actions.
(emphasis added)

In view of the above, applicants believe that the presently claimed invention is unobvious over Nakamura.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their

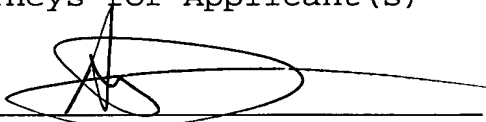
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allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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